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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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MARSHALL, GERSTEIN & BORUN LLP
6300 SEARS TOWER
233 S. WACKER DRIVE
CHICAGO, IL 60606

EXAMINER	
MARVICH, MARIA	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,972	BARTLETT, JEFFREY S.	
	Examiner	Art Unit	
	Maria B Marvich, PhD	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *13-16,19,20,27-34 and 36-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,17,18 and 21-23* is/are rejected.

7)☒ Claim(s) *24-26 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office action is in response to a Response to a Restriction Requirement filed 11/28/03. Claims 1-41 are pending in this application. Claims 13-16, 19-20, 27-34 and 36-41 are withdrawn from consideration as being drawn to nonelected inventions, Claims 1-12, 17-18, 21-26 and 35 are examined herein.

Election/Restrictions

Applicant's election with traverse of Group I (Claims 1-12, 17-18, 21-26 and 35) in the amendment filed 11/28/03 is acknowledged. Applicants have traversed the restriction requirement of Groups I and IV and Groups I and V. As group I and IV and V are related as product and process claims, applicants requested that if the product claims are found allowable, the process claims be rejoined with the product claims.

The following guidelines are used in the event that the product claims be found allowable.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection

are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The requirement between the remaining groups is still deemed proper and is therefore made FINAL. Therefore, an examination of claims 1-12, 17-18, 21-26 and 35 follows in so much as they read on SEQ ID 10. Claims 13-16, 19-20, 27-34 and 36-41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claim Objections

Claims 11-12 and 21-23 are objected to in as much as they are drawn to non-elected subject matter as they recite non-elected subject matter, that is they read on non-elected sequences and on non-elected AAV vectors, and should be redrafted without said subject matter.

Claims 24-26 and 35 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiply dependent claim. See MPEP § 608.01(n). Accordingly, the claims not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 17-18 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an AAV2 vector with an amino acid insertion following amino acids 139, 161, 459, 584, 588 and 657, does not reasonably provide enablement for ANY AAV vector other than AAV2 with insertions at these sites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without

undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is not based on a single factor but is rather a conclusion reached by weighing many factors (See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter, 1986) and In *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988); these factors include the following:

1) Nature of invention. The invention recites an AAV vector comprising a capsid protein with an amino acid insertion in the capsid. The amino acid insertion can be a targeting peptide such as CDCRGDCFC (SEQ ID NO 10). This invention requires a complex combination of molecular cloning in combination with viral and cell culture techniques to generate the recombinant adenovirus.

2) Scope of the invention. The invention recites very specific sites for insertion such as after amino acid 139, 161, 459, 584, 588 and 657 in AAV. The lack of identification of sites in any AAV other than AAV2 renders the ability to determine the sites of any AAV unpredictable.

3) Number of working examples and guidance. The instant specification teaches means of constructing and analyzing AAV2 with an amino acid insertion following amino acids 139, 161, 459, 584, 588 and 657. Applicants teach that surface and secondary structural regions that could serve as sites of insertion of amino acids were identified in a comparison of five parvoviruses. Following this, site-directed mutagenesis of AAV2 was used to identify the specific sites of insertion was not used to identify the regions of insertion (see example 1, page 11-12. Applicants teach that these sites can be understood to be corresponding sites in other parvovirus (see e.g. page 4, line 3-12).

4) State of the art. There has been much interest in the development of viruses that transduce therapeutic genes into specific target tissues. Manipulation of AAV for altered tropism is a new and developing art.

5) Unpredictability of the art. Chiorini et al teach the relationship of AAV4 and AAV3 to AAV2 (Journal of Virology, 1997 see Figure 3 and page 6828, column 2). The relationships between the capsid proteins are 62% and 63% and to Moscovy duck and goose 53% homology while to other autonomous parvovirus there is little homology (page 6828, column 2, paragraph 3,line1-7).

6) Amount of Experimentation Required. The invention recites an AAV vector comprised of an amino acid insertion following amino acids 139, 161, 459, 584, 588 and 657 which correlate to sites of AAV2. In view of the unpredictability of the art of identifying the same sites in any other AAV vector: undue experimentation would be required to practice the claimed methods with reasonable expectation of success, absent a specific and detailed description in the specification. The level of skill in the art covering this invention was high at the time of invention; however, given the unpredictability of the art, the poorly developed state of the art, the lack of working examples and the lack of guidance provided by applicants, the skilled artisan would have to have conducted undue experimentation to practice the claimed invention.

Claims 1-12, 17-18 and 21-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim an AAV vector with an amino acid insertion at specific amino acid sequences with a critical element that peptides or polypeptides of interest may be inserted for presentation in a desired conformation to allow for the development of AAV vectors that deliver DNA to specific target cells or display surface immunogenic peptides or polypeptides (see e.g. page 3,line 18-22).

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus. In the instant invention, applicants recite that these sites are in positions following amino acids 139, 161, 459, 584, 588 or 657 in the VP1 capsid which sequence is presented in SEQ ID NO 13. This sequence corresponds to VP1 of AAV2. Applicants teach that surface and secondary structural regions were identified in a comparison of five parvoviruses. However, this broad and hypothetical functional characteristic was not used to identify the specific sites of AAV that could tolerate insertion mutagenesis and provide for presentation of peptides for targeting or immunogen presentation. Rather site-directed mutagenesis of AAV2 was used to identify the specific sites of insertion was not used to identify the regions of insertion (see example 1, page 11-12). However, the structural requirements of this region to meet the functional limitations of

the claimed invention are unknown. Applicants teach that these sites can be understood to be corresponding sites in other parvovirus (see e.g. page 4, line 3-12). Neither applicant nor the prior art provide a correlation between the structure of any parvovirus VP1 protein and the functional requirements for identification of sites for insertion of a peptide for representation of targeting motifs or immunogens. Chiorini et al teach the relationship of AAV4 and AAV3 to AAV2 (Journal of Virology, 1997 see Figure 3 and page 6828, column 2). The relationships between the capsid proteins are 62% and 63% and to Moscovy duck and goose 53% homology while to other autonomous parvovirus there is little homology (page 6828, column 2, paragraph 3,line1-7). It is unclear what functional characteristics should be used to identify the sites of insertion for vectors other than AAV2. In an unpredictable art, the disclosure of one species would not represent to the skilled artisan a representative number of species sufficient to show applicants were in possession of claimed genus. Given the diversity of parvovirus capsid regions and the lack of written disclosure of the structural characteristics, and the lack of written disclosure of the functional characteristics required for the insertion sites to be identified in other parvovirus, it is concluded that applicant was not in possession of their invention.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria B Marvich, PhD whose telephone number is (703) 605-1207. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maria B Marvich, PhD
Examiner
Art Unit 1636

December 22, 2003

REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600